REMARKS/ARGUMENTS

Upon entry of this amendment, claims 1, 2, 6, 9-16, 19, and 47 are pending in this application and are presented for examination. Claims 1, 6, and 12 have been amended. No new matter has been introduced with the foregoing amendments. Support for amended claim 1 is found, for example, on page 7, lines 16-18 and page 34, lines 7-31. Support for amended claim 6 is found, for example, on page 17, lines 24-31. Support for amended claim 6 is found, for example, on page 19, lines 12-29. Thus, no new matter has been introduced. Reconsideration is respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

A. Written description

Claims 1-16, 19, and 47 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Examiner alleges that the recitation "TRAC1 polypeptide comprising **an** amino acid sequence having at least 90% identity to **an** amino acid sequence of SEQ ID NO: 1" encompasses virtually any protein, [and if] interpreted as broadly as is reasonable . . . reads on an extremely large genus of polypeptides . . . with broad functional limitations and virtually no structural limitations". The Examiner further alleges that the "Applicants' claims have virtually no structure/function activity basis". *See* Office Action at page 4. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

In order to expedite prosecution, Applicants have amended the claims to recite, in part, "a TRAC1 polypeptide, wherein the polypeptide comprises an amino acid sequence having at least about 90% identity to *the* amino acid sequence of SEQ ID NO:1, *wherein the TRAC1 polypeptide has ligase activity*". (Emphasis added.) By virtue of this amendment, the claims now read on a genus of polypeptides with 90% identity to *the* amino acid sequence of SEQ ID NO: 1. The amended claims now also read on polypeptides with TRAC1 ligase activity. Applicants assert that the amended claims fully comply with the requirements for written

description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). (This case was discussed in detail in the previous Office Action response.) The claims as amended provide a recitation of structural features common to the members of the genus, namely, 90% identity to the amino acid sequence of SEQ ID NO: 1, and a function ascribable to the members of this genus. Thus, contrary to the Examiner's rejection, the claims do not read on "an extremely large genus of genus of polypeptides . . . with broad functional limitations and virtually no structural limitations. Furthermore, the claims, which recite a specified percent identity and function, would "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*quoting Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 111, 1116 (Fed. Cir. 1991)).

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the written description rejection under 35 U.S.C. § 112, first paragraph.

B. Enablement

Claims 1-16, 19 and 47 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner alleges that the instant specification, while being enabling for a method comprising contacting a compound with a TRAC1 polypeptide having the amino acid sequence of SEQ ID NO:1, does not reasonably provide enablement for any method comprising contacting a compound with any TRAC1 polypeptide comprising **an** amino acid sequence having at least 90% identity to **an** amino acid sequence of SEQ ID NO: 1. (Emphasis added by Examiner.) *See* page 5 of the Office Action. The Examiner further alleges that "while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutatgenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants (i.e., encoding a ligase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property." *See* page 7 of the Office Action. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

In order to expedite prosecution, Applicants have amended the claims to recite, in part, "a TRAC1 polypeptide, wherein the polypeptide comprises an amino acid sequence having at least about 90% identity to *the* amino acid sequence of SEQ ID NO:1, *wherein the TRAC1 polypeptide has ligase activity* . . .". (Emphasis added.)

Applicants respectfully submit that the claims as amended are fully enabled by the specification. Methods for determining percent identity are disclosed in the specification, thus enabling a skilled artisan to identify "a TRAC1 polypeptide comprising an amino acid sequence having at least 90% identity to *the* amino acid sequence of SEQ ID NO: 1". Furthermore, the claims now recite that the TRAC1 polypeptide has ligase activity. Methods for determining ligase activity are known in the art as disclosed in the specification. *See* page 9, lines 32-34 of the specification. Thus, given the high skill level in the biotechnological arts, the skilled artisan could readily identify "a TRAC1 polypeptide, wherein the polypeptide comprises an amino acid sequence having at least about 90% identity to *the* amino acid sequence of SEQ ID NO:1, wherein the TRAC1 polypeptide has ligase activity", using the disclosure in the specification and routine methods in molecular biology and biochemistry without undue experimentation.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph.

CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 1-4, 6-10, 13-16, 19, and 47 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,180,662 ("Sitkovsky"). To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

In making this rejection, the Examiner alleges that "Sitkovsky specifically teaches a method comprising contacting a compound with a "'TRAC1 polypeptide or a fragment thereof' . . . and determining the 'functional effect' of the compound upon the 'TRAC1 polypeptide'". The Examiner states that "[a] specific or general teaching of the TRAC1 polypeptide is unnecessary to anticipate the methods claimed [because] the cells of the methods taught by Sitkovsky

inherently comprise the defined 'TRAC1 polypeptides'. Thus, the methods taught by Sitkovsky anticipate the claimed methods drawn to contacting a compound with a TRAC1 polypeptide." (Emphasis added.) *See* Office Action at pages 11-12. The Examiner then concludes that "measuring secreted granule-associated BLT esterase activity" as taught by Sitkovsky is considered to be encompassed by "determining the functional effect of the compound upon the TRAC1 polypeptide" as claimed in the present invention. *See* Office Action at page 12.

Applicants respectfully disagree with the Examiner's interpretation of what is fairly disclosed by inherency from the teachings of Sitkovsky. The Examiner appears to suggest that the teachings in Sitkovsky would inherently anticipate any gene or polypeptide that is expressed in T lymphocytes and which is involved with T lymphocyte activation, whether or not such a gene or polypeptide is known. In order for a claim element to be anticipated by a prior art reference, "the missing descriptive material must be necessarily present in the thing described in the reference, and that it would be so *recognized* by persons of ordinary skill". (Emphasis added.) *See Continental Can, Co. v. Monsanto Co.*, 948 F.2d 1264, 1268-1269 (Fed. Cir. 1991). Furthermore, "[i]n relying upon a theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *See* MPEP §2112 (emphasis in original), quoting *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

Here, even *if* TRAC1 was expressed in the T lymphocytes described by Sitkovsky, the skilled artisan would have no way of recognizing this because TRAC1 is not disclosed in Sitkovsky, much less polypeptides with at least 90% identity. Even less readily recognizable is the fact that TRAC1 is involved in T lymphocyte activation. The role of TRAC1 in mediating T lymphocyte activation could not have been recognized before the discoveries of the instant application were made. Absent a disclosure of TRAC1, it would be harder still to recognize any of the activities exhibited by TRAC1 polypeptide as disclosed by the present invention. Furthermore, the Examiner has failed to allege how knowledge of the role of TRAC1

in T-lymphocyte activation or TRAC1 activities would necessarily flow from the teachings of Sitkovsky. At most, the Examiner only suggests that all T lymphocytes express TRAC1, without presenting data to support this suggestion. Simply put, the skilled artisan would not have been able to recognize that which was unknown about the activation of T lymphocytes. To argue otherwise would be to suggest that Sitkovsky inherently teaches any future components of the T lymphocyte activation pathway yet to be discovered. The MPEP and Federal Circuit case law does not allow the reach of inherency to be thus extended.

From the foregoing, it is the Applicants' belief that Sitkovsky neither expressly or inherently discloses each and every element of the claimed invention. However, in order to expedite prosecution, Applicants have further distinguished the claimed invention from the teachings of Sitkovsky by amending the claims to recite, in part, "determining the functional effect of the compound upon TRAC1 polypeptide activity". As discussed above, Sitkovsky does not disclose TRAC1 polypeptide or any specific TRAC1 activities. Specifically, Sitkovsky fails to disclose SEQ ID NO: 1 or any disclosure of the activities of TRAC1 such as ligase activity or induction of CD69 expression, among others disclosed in the present invention. The claims as amended are now drawn to a method of screening for agents that modulate T lymphocyte activation that relies on determining a functional effect on *TRAC1 activity*, a feature of which Sitkovsky is slient. While Sitkovsky discloses the activation of T lymphocytes with activating stimuli, it fails to demonstrate any connection or involvement of TRAC1 in the induction of the marker used in Sitkovsky, secreted granule-associated BLT esterase activity. Because multiple and diverse signal transduction pathways are activated in T lymphocytes upon activation, one of skill in the art would not necessarily (nor could they) recognize any connection between secreted granule-associated BLT esterase activity and TRAC1 activity based on the disclosure in Sitkovsky. Sitkovsky does not contemplate an association between T lymphocyte activation and TRAC1 activity. Rather, Applicants respectfully submit that Sitkovsky can only be read to teach a method for measuring T-lymphocyte activation by measuring the *secretion of granule-associated BLT esterase activity* after treatment with activating stimuli and screening

methods based on this activity. Thus, Sitkovsky fails to teach or suggest methods for the screening of compounds that have a effect on *TRAC1 polypeptide activity* as is presently claimed.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 102(b).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

Gene H. Yee

Gene H. Yee
Reg. No. 57,471

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
GHY/lls
60956240 v1